Off-pump coronary artery bypass sacrifices graft patency: Meta-analysis of randomized trials

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The most recent meta-analysis[1] of 37 randomized trials of off-pump coronary artery bypass (OPCAB) versus conventional coronary artery bypass grafting (CABG) demonstrated that mortality, stroke, myocardial infarction, and renal failure were not reduced in OPCAB; however, selected short-term and midterm clinical and resource outcomes were improved compared with CABG. The previous cumulative analysis (by Parolari and associates[2]) of 5 prospective randomized studies (by Nathoe,[3] Khan,[4] Puskas,[5] Widimsky,[6] Lingaas,[7] and their associates) then available in the literature, however, documented a reduction in postoperative patency of bypass grafts performed during OPCAB procedures. Since the meta-analysis by Parolari and associates[2] was conducted, Lingaas and colleagues[8] have updated the 3-month patency,[7] and Kobayashi and coworkers[9] and Al-Ruzzeh and associates[10] have reported results of other randomized controlled trials. In these trials,[8-10] OPCAB provided the same angiographic graft patency as CABG, despite the conclusion of the meta-analysis by Parolari and colleagues.[2] To reassess differences in graft patency between OPCAB and CABG, we performed a meta-analysis of currently available randomized controlled trials of OPCAB versus CABG.

Materials and Methods

All prospective randomized controlled trials that compared patency at least 3 months after OPCAB and CABG were identified using a 2-level search strategy. First, a public domain database (MEDLINE) was searched with a Web-based search engine (PubMed). Second, relevant studies were identified through a manual search of secondary sources including references of initially identified articles. The MEDLINE database was searched from January 1966 to June 2006. Keywords included "off-pump," "off pump," "opcab," "patency," and "randomized controlled trial." Studies considered for inclusion met the following criteria: The design was a prospective randomized controlled clinical trial; patients were randomly assigned to OPCAB versus CABG; and main outcomes included at least 3-month graft patency evaluated by angiography. All qualifying studies were assessed for adequate blinding of randomization, completeness of follow-up, and objectivity of the outcome assessment. Data regarding arterial graft and venous graft (excluding radial artery graft as available) patency were abstracted from each individual study. For each study, data regarding patency in both the OPCAB and CABG groups were used to generate risk ratios (RRs) (<1, favors OPCAB; >1, favors CABG) and risk differences (RDs) (<0, favors OPCAB; >0, favors CABG) for graft "occlusion" and 95% confidence intervals (CIs). Study-specific estimates were combined with a random-effect model. Between-study heterogeneity was analyzed by standard χ^2 tests. Sensitivity analyses were performed to assess the contribution of each study to the pooled estimate by excluding individual trials one at a time and recalculating the pooled RR and RD estimates for the remaining studies. Publication bias was assessed graphically with a funnel plot and mathematically with an adjusted rank-correlation test.

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Results

Our search identified 6 prospective randomized controlled clinical trials[3-6,8,10] (Table 1). We excluded the trial by Kobayashi and associates[9] because these workers merely examined early (within 3 weeks after the operation) graft patency. Allocation concealment and blinding were not possible in these trials given that the intervention was surgical; however, all trials used a blinded committee for adjudication of events. Careful accounting for dropouts and crossovers was provided in all cases, and all but one analysis[5] were conducted by intention-to-treat. All of the 6 individual trials demonstrated a statistically nonsignificant benefit of CABG over OPCAB for overall graft patency. Pooled analysis demonstrated a statistically significant 27% increase in overall graft "occlusion" with OPCAB relative to CABG (RR, 1.27; 95% CI, 1.03-1.56; $P = .0234$) (RD, 3.0%; 95% CI, 0.6%-5.4%; $P = .0129$). There was neither trial heterogeneity of results nor evidence of significant publication bias. Exclusion of any single trial from the analysis did not substantively alter the overall result of our analysis. Subanalyses demonstrated a statistically nonsignificant benefit of CABG over OPCAB for arterial graft patency (RR, 1.17; 95% CI, 0.62-2.24; $P = .6259$) (RD, 2.0%; 95% CI, −1.2%-5.2%; $P = .2195$) and a statistically significant 28% increase in venous graft "occlusion" with OPCAB relative to CABG (RR, 1.28; 95% CI, 1.06-1.54; $P = .0094$) (RD, 4.0%; 95% CI, 0.2%-7.8%; $P = .0396$).

Discussion

The present meta-analysis demonstrated a significant increase in overall graft "occlusion," especially in venous graft "occlusion," with OPCAB relative to CABG. On the one hand, OPCAB de-

TABLE 1. Characteristics of trials and meta-analysis of graft patency

	Al-Ruzzeh[10]	Lingaas[8]	Widimsky[6]	Puskas[5]	Khan[4]	Nathoe[3]	Combined
No. of patients	168	120	400	197	103	110	1098
Timing of CAG, mo	3	12	12	12	3	12	9
Patients undergoing CAG, %	90	91	64	78	80	64	75
Patients features	Isolated, elective CAS	Elective CAS	Isolated, elective CAS	Isolated, primary, elective CAS	Isolated, primary, CAS	Isolated, primary, elective CAS	
Intention-to-treat	No crossovers	Yes	No	Yes	Yes	Yes	
Events committee	Blinded	NR	NR	Blinded	Blinded	Blinded	
Arterial graft patency							
OPCAB, n/N* (%)	111/113 (98)† (50/55 [91])§	48/51 (94)†	98/107 (91)†	95/101 (94)‡	46/50 (92)† (26/34 [76])§	NR	398/422 (94)
CABG, n/N* (%)	111/114 (97)† (44/50 [88])§	54/56 (96)†	100/110 (91)†	102/104 (98)‡	47/47 (100)† (22/22 [100])§	NR	414/431 (96)
RR‖ (95% CI)	0.67 (0.11-3.95)	1.65 (0.29-9.46)	0.93 (0.39-2.19)	3.09 (0.64-14.95)	—	—	1.17 (0.62-2.24)
RD¶ (95% CI), %	−0.9 (−4.7-3.0)	2.3 (−5.8-10.4)	−0.7 (−8.2-6.8)	4.0 (−1.3-9.3)	8.0 (0.5-15.5)	—	2.0 (−1.2-5.2)
Venous graft patency							
OPCAB, n/N* (%)	50/61 (82)	67/84 (80)	86/176 (49)	140/150 (93)	40/44 (91)	NR	383/515 (74)
CABG, n/N* (%)	60/68 (88)	84/97 (87)	145/246 (59)	147/156 (94)	56/59 (95)	NR	492/626 (79)
RR‖ (95% CI)	1.53 (0.66-3.56)	1.51 (0.78-2.92)	1.25 (1.01-1.53)	1.16 (0.48-2.76)	1.79 (0.42-7.58)	—	1.28 (1.06-1.54)
RD¶ (95% CI), %	6.3 (−6.0-18.6)	6.8 (−4.1-17.8)	10.1 (0.5-19.7)	0.9 (−4.5-6.3)	4.0 (−6.2-14.2)	—	4.0 (0.2-7.8)
Overall graft patency							
OPCAB, n/N* (%)	161/174 (93)#	115/135 (85)	197/283 (70)	235/251 (94)‡	86/94 (91)#	63/69 (91)	857/1006 (85)
CABG, n/N* (%)	171/182 (94)#	138/153 (90)	264/356 (74)	249/260 (96)‡	103/106 (97)#	83/89 (93)	1008/1146 (88)
RR‖ (95% CI)	1.24 (0.57-2.68)	1.51 (0.81-2.83)	1.18 (0.92-1.51)	1.51 (0.71-3.18)	3.01 (0.82-11.01)	1.29 (0.43-3.83)	1.27 (1.03-1.56)
RD¶ (95% CI), %	1.4 (−3.8-6.6)	5.0 (−2.6-12.6)	4.6 (−2.5-11.6)	2.1 (−1.7-6.0)	5.7 (−0.8-12.1)	2.0 (−6.5-10.4)	3.0 (0.6-5.4)

CABG, Conventional coronary artery bypass grafting; CAG, coronary angiography; CAS, coronary artery surgery; CI, confidence interval; NR, not reported; OPCAB, off-pump coronary artery bypass; RD, risk difference; *RR*, risk ratio. *No. of patent grafts/Total No. of grafts. †Patency of internal thoracic artery grafts. ‡Patency including radial artery grafts. §Patency of radial artery grafts. ‖Risk ratio for graft "occlusion" (<1, favors OPCAB; >1, favors CABG). ¶Risk difference for graft "occlusion" (<0, favors OPCAB; >0, favors CABG). #Patency excluding radial artery grafts.

creases arterial fibrillation, transfusion, inotrope requirements, respiratory infections, ventilation time, intensive care unit stay, and hospital stay.[1] At the expense of graft patency, dare we perform OPCAB rather than CABG to merely improve these selected clinical and resource outcomes?

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